Violence in psychosis: conceptualizing its causal relationship with risk factors

Jelle Lamsma[a] and Joke M. Harte[a,b]

[a] Department of Criminal Law and Criminology, VU University Amsterdam, the Netherlands

[b] NSCR, The Netherlands Institute for the Study of Crime and Law Enforcement, Amsterdam, the Netherlands

DOI: 10.1016/j.avb.2015.05.003

Abstract

Background While statistically robust, the association between psychosis and violence remains causally unexplained.

Objective To provide an overview of possible causal pathways between risk factors and violence in psychosis.

Methods A structured narrative review of relevant studies published between 1990 and 2013, found via online databases and bibliographies. Both reviews and empirical studies were included. No restrictions were applied to language, study design, sample characteristics and measurement of psychosis and violence. Case reports and studies about self-harm were excluded. A final sample of 69 studies was used.

Findings The lack of knowledge regarding the causal relationship between psychosis and violence is partially due to methodological aspects of research. These aspects include study design, sampling, operationalization and confounding variables. Moreover, violence is the potential outcome of several interrelated risk factors: demographics, social factors, persecutory delusions, command hallucinations, comorbid antisocial personality pathology, substance use, inadequate insight, treatment non-adherence and physiological factors. Forty-one possible causal pathways between these risk factors and violence are presented.

Conclusions This study stimulates research by providing a theoretical framework, avenues for future investigation and methodological recommendations. Understanding violence in psychosis enhances its prevention and treatment, decreases stigma associated with psychosis and improves the patient's legal position.

1. Introduction

Psychosis is a heterogeneous syndrome, described in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) as comprising delusions, hallucinations, diminished emotional expression as well as disorganized thinking and motor behavior. These symptoms are often associated with a mental disorder, such as schizophrenia, delusional disorder and schizoaffective disorder. Psychosis may also arise as a result of substance use and other medical conditions, including cerebrovascular, endocrine and neoplastic diseases, epilepsy and head trauma.

Since the 1990s, a large number of studies have found a positive and statistically robust association between psychosis and violence (Angermeyer, 2000; Bo, Abu-Akel, Kongerslev, Haahr & Simonsen, 2011; Douglas, Guy & Hart, 2009; Fazel, Gulati, Linsell, Geddes & Grann, 2009; Hodgins, 2008; Joyal, Dubreucq, Gendron & Millaud, 2007; Modestin, 1998; Nederlof, Muris & Hovens, 2013; Volavka, 2013; Walsh, Buchanan & Fahy, 2002). Prevalence rates of violent behavior among schizophrenia patients reported by recent large-scale prospective studies conducted in the United States and Sweden range between 9.20% and 19.60% (Elbogen & Johnson, 2009; Fazel, Grann, Carlström, Lichtenstein & Långström, 2009; Swanson et al., 2006). A meta-analysis of 204 studies found that in people diagnosed with psychosis the odds of violence are 49.00% to 68.00% higher relative to the odds of violence in people without such a diagnosis (Douglas et al., 2009). In another meta-analysis, Fazel, Gulati et al. (2009) report that schizophrenia and other psychoses are associated with an odds ratio for violence of 4.00 (95% CI [3.00, 5.30]) in men, compared with 7.90 (95% CI [4.00, 15.40]) in women. The population-attributable risk for violence in schizophrenia has been estimated at less than 10.00% (Walsh et al., 2002). Understanding violent behavior in psychotic patients is important for at least three reasons. Firstly, it may reduce such behavior – and the emotional and financial costs that come with it – by facilitating more effective prevention and treatment (Douglas et al., 2009; Hodgins,

2008; Volavka, 2013). Secondly, it may help to decrease stigma associated with the syndrome. Psychotic patients are often perceived as dangerous, while *de facto* only a small proportion of them act violently (Douglas et al., 2009; Hodgins, 2008; Joyal et al., 2007; Markowitz, 2011; Walsh et al, 2002). Thirdly, it serves to protect the civil rights of psychotic individuals by improving risk assessment in cases of civil and criminal commitment (Douglas et al., 2009).

Numerous factors have been proposed to account for the increased risk of violence in psychosis, with examples being low socioeconomic standing, substance use, symptomatology and deficient insight. However, little is known about the mechanisms by which such risk factors may cause violent behavior in psychotic patients (Bo et al., 2011; Douglas et al., 2009; Witt, van Dorn & Fazel, 2013). In other words, studies have yet to move from correlation to causation. Moreover, prevailing hypotheses on this topic have not been the object of broad-gauged review. The main purpose of the present study is therefore to provide an overview of possible causal pathways between the most replicated risk factors and violent behavior in psychosis. To this aim, a structured narrative review of the relevant literature is presented. Methodological issues of research in this field will be outlined first. The most replicated risk factors for violence in psychosis and possible causal pathways are subsequently examined. Finally, the study's limitations are discussed in conjunction with its implications for future research and practice.

2. Methodology

A narrative review was conducted of studies found using an explicit search strategy with a set of inclusion criteria. A narrative review was chosen over a systematic review. Whereas a systematic review includes all traceable papers selected according to a strict protocol in order to evaluate findings in relation to methodological quality, a narrative review takes a more liberal

and broader approach useful for synthesizing the current body of knowledge in a certain research area and developing a theoretical framework (Cronin, Ryan & Coughlan, 2008; Marriot, Hamilton-Giachritsis & Harrop, 2013). The latter approach is consistent with the review's principal objective, which is to conceptualize the causal relationships between risk factors and violence in psychosis rather than to rigorously evaluate empirical evidence. Besides, most risk factors presented here have been well described in previous reviews[1].

2.1. Search strategy

The online databases of PubMed, PsycINFO, ScienceDirect and Google Scholar were searched for studies published between 1990 and 2013. Search terms covered psychosis (viz. "psychot*", "psychos*", "schizo*", "mental*"), violence (viz. "violen*", "aggress*", "hosti*", "crim*", "offend*") and risk factors generically (viz. "risk*", "correlat*", "variable*", "predict*"). Additional searches were performed for specific risk factors (e.g. "gender", "hallucinations", "substance", "insight"). Other studies were found by manually searching relevant bibliographies.

2.2. Inclusion criteria

Both review articles and empirical studies were considered for inclusion, as long as they reported on risk factors for violence in psychosis. We chose to include and emphasize findings of reviews as they are generally considered to be more valid than those of individual empirical

[1] For systematic reviews on risk factors for violence in psychosis, see Douglas et al. (2009), Fazel, Gulati et al. (2009), Nederlof et al. (2013) and Witt et al. (2013).

studies. Moreover, authors may posit relevant hypotheses in either type of study. For the same reason, no restrictions were made relating to language, study design (i.e. cohort, case-control and cross-sectional), the type of sample used (i.e. prison, psychiatric, community), age of participants and measurement of psychosis (i.e. self-report, unstructured and structured interview) and violence (i.e. criminal records, case notes, collateral information and self-report). Case reports and studies using self-harm as the sole outcome measure were excluded. Studies were eligible irrespective of whether psychosis was associated with a mental disorder (e.g. schizophrenia, delusional disorder), substance use or other medical condition (e.g. brain tumor, epilepsy). Studies examining specific symptoms of psychosis (e.g. delusions, hallucinations) were also included. Following the structured search, 66 studies were selected. Three studies were added to provide hypotheses not presented in the literature obtained through the structured search. This brought the total number of studies used in this review to 69.

3. Findings

3.1. Methodological issues in research on violence in psychosis

The association between psychosis and violence has been found across different study designs and settings. However, several methodological aspects of research may affect the size of this association and thwart comparison between studies (Bo et al., 2011; Douglas et al., 2009; Nederlof et al., 2013). The following aspects require attention: study design, sampling, operationalization of variables and confounding factors.

3.1.1. Study design and sampling

Since it is impossible or unethical to expose study subjects to relevant risk factors (e.g. neighborhood of residence, psychotic symptoms, substance use), research on psychosis and violence is necessarily observational in nature and more subject to bias than experimental research. Three types of observational study design can be distinguished and ordered according to the validity of their results: cohort, case-control and cross-sectional (Mann, 2003). Establishing a causal relationship between two events is conditional on knowing their sequential order and temporal proximity. This is only possible in cohort studies, in which variables of interest are measured chronologically in people who share a common characteristic (e.g. year of birth, diagnosis of schizophrenia) (Mann, 2003). As study subjects who demonstrate the outcome of interest are drawn from the same population as those who do not, confounding bias is minimized when comparing the two groups (see paragraph 3.1.4.). The risk of sampling bias is reduced, because participants are selected prior to demonstrating the outcome of interest. While convenient and efficient for studying a rare phenomenon such as psychosis, samples consisting of only discharged psychiatric patients could be selective, however (see below). Findings may also be biased by attrition at follow-up, which is often related to the variables under study. Case-control studies compare two or more groups of people differing on an outcome variable with respect to attributes hypothesized to cause these group differences. This retrospective measurement gives rise to several kinds of bias. Firstly, temporal bias, when it is uncertain whether the independent variable preceded and approximated the dependent variable in time. Secondly, biased reporting by patient and researcher if they are not blind which study group (i.e. case or control) the former belongs to. Finally, because selection of study subjects is based on the outcome of interest, sampling is prone to bias (Mann, 2003). It is also important that cases and controls do not systematically differ on one or more unmeasured qualities that confound the association between measured risk factors and violence. While it is unfeasible to

find perfectly matching study groups or statistically control for all potential confounders, researchers should compare violent psychotic individuals to non-violent people with similar risk profiles, preferably siblings or other psychotic patients. However, the composition of comparison groups varies considerably across studies and often includes arguably less comparable subjects, such as general population controls and non-psychotic psychiatric patients (Douglas et al., 2009; Walsh et al., 2002). Cross-sectional research does not allow for the inference of causality, as variables are measured within one study group at a single point in time (Mann, 2003). Probably owing to the high cost and duration of cohort studies, most research on violence in psychosis involves case-control and cross-sectional studies (Bo et al., 2011; Douglas et al., 2009; Fazel, Gulati et al., 2009; Nederlof et al., 2013; Walsh et al., 2002). To illustrate this point, Fazel, Gulati et al. (2009) identified in their meta-analysis of 20 studies only 3 cohort studies in which violence was measured after a diagnosis of schizophrenia or other psychosis was made. Clearly, more high-quality cohort studies are needed to advance this field of research.

Many studies draw samples from populations of patients institutionalized in correctional or psychiatric facilities (Douglas et al., 2009; Walsh et al., 2002). These samples may be selective, since psychotic individuals who are convicted or hospitalized may be different from those who are not. At the same time, institutionalized patients are often underrepresented in community samples (Walsh et al., 2002). Thus, combined sampling is *ne plus ultra*.

3.1.2. Definition and measurement of violence

Definitions of violence vary widely (Bo et al., 2011; Douglas et al., 2009; Walsh et al., 2002). Some studies only count physical acts, which may range in seriousness from pushing to homicide, while others incorporate verbal behavior as well. Questionable definitions can also be

found, such as those including self-harm and vandalism. A number of studies fail to give any definition of violence (Bo et al., 2011; Douglas et al., 2009).

The most common data sources for the measurement of violence are criminal records, case notes, collateral information and self-report (Douglas et al., 2009; Walsh et al., 2002). It is advisable to use these methods in combination, because the information contained in each of them is often incomplete or selective: characteristics of the justice and mental health care systems, suspect and offense all determine the number and type of convictions; information in case notes is recorded only when relevant for the patient's criminal case, probation officer or clinician; the patient's family or friends may be ignorant of violent incidents or have conflicting interests; the reports of patients themselves may be affected by fear of negative consequences, social desirability and deficient and biased recall (see also Walsh et al., 2002).

3.1.3. Definition and measurement of psychosis

Psychosis is variably defined in studies (Bo et al., 2011; Douglas et al., 2009; Nederlof et al., 2013; Walsh et al., 2002). It is sometimes part of the broad concepts of Major Mental Disorder (MMD) or Severe Mental Illness (SMI), which include different mental disorders, such as schizophrenia and depression (e.g. Hodgins, 1995; Modestin & Wuermle, 2005; Tiihonen, Isohanni, Räsänen, Koiranen & Moring, 1997). Other studies examine disorders of which psychotic symptoms are pathognomonic, such as schizophrenia or schizophreniform disorder (e.g. Arseneault et al., 2003; Hodgins, Hiscoke & Freese, 2003), or the syndrome of psychosis as a whole (e.g. Moran et al., 2003). A last category of studies looks at specific symptoms of psychosis, most notably delusions and hallucinations (e.g. Coid et al., 2013; Fresan et al., 2005). Since psychosis is a heterogeneous syndrome with variable causes, symptom-level research seems most appropriate (Bo et al., 2011; Douglas et al., 2009).

Methods for diagnosing psychosis range from self-report to unstructured and structured interviews (Bo et al., 2011; Douglas et al., 2009; Walsh et al., 2002). Structured interviews are considered the most reliable and valid means of assessment. Because self-report measures are contingent on the patient's level of self-insight, defensiveness and malingering, their validity is often limited (Sternberg, Roediger & Halpern, 2007). In addition, they typically do not contain questions regarding symptoms of psychosis (Douglas et al., 2009). While the quality of diagnoses based on unstructured interviews is improved when complemented with clinical observation, collateral information or the patient's medical history, they have poor inter-rater reliability and validity compared with structured interviews (Walsh et al., 2002). In structured interviews, the same information is collected from each patient with a standardized protocol whereby different interviewers are likely to reach similar conclusions (Sternberg et al., 2007). The diagnostic accuracy of structured interviews has empirically been proven superior to that of unstructured interviews (Douglas et al., 2009; Sternberg et al., 2007).

3.1.4. Confounding factors

It is possible that psychosis and violence are not causally related, but the shared result of a third factor (Bo et al., 2011; Douglas et al., 2009). Comorbid antisocial personality pathology and substance use have frequently been suggested as potential confounders (e.g. Fazel, Långström, Hjem, Grann & Lichtenstein, 2009; Tengström, Hodgins, Grann, Långström & Kullgren, 2004). Nonetheless, it appears that specific psychotic symptoms at least partially account for the syndrome's association with violence (see paragraph 3.2.3.). Other of-cited possibilities include the aforementioned methodological factors, deinstitutionalization and discrimination by health care or justice systems (e.g. Hodgins, 2008; Joyal et al., 2007; Markowitz, 2011; Mullen, 2006; Nederlof et al., 2013). However, it is unlikely that these factors fully mediate the association between psychosis and violence, since this association has been observed across different time

periods, locations and study designs (Hodgins, 2008; Wallace, Mullen & Burgess, 2004). A final possible confounding factor is publication bias. Unfortunately, few studies have investigated this possibility (e.g. Douglas et al., 2009; Witt et al., 2013).

3.2. Possible causal pathways between risk factors and violence in psychosis

The following risk factors for violence in psychosis are most commonly cited in the literature: demographic factors, social factors, persecutory delusions and command hallucinations, comorbid antisocial personality pathology, substance use, inadequate insight, treatment non-adherence and physiological factors.

3.2.1. Demographic factors

Demographic factors most frequently associated with violence in psychotic patients are male gender, young age, single status, homelessness, unemployment, low educational attainment, low socioeconomic status, belonging to an ethnic minority, past hospitalization for psychosis and past conviction of violent crime (Bo et al., 2011; Modestin, 1998; Rogers & Fahy, 2008; Witt et al., 2013). It is unclear how these factors causally relate to violence. Some may predispose patients toward violent behavior by reason of low self-control, such as male gender and young age (Gottfredson & Hirschi, 1990). The effect of most demographic factors is probably indirect, since the association between violent behavior and psychosis has been shown to remain when these are controlled for (Joyal et al., 2007; Markowitz, 2011; Modestin, 1998). However, this finding has not been subject of systematic research. Perhaps low socioeconomic status and unemployment reflect conditions of social disorganization (see paragraph 3.2.2.). An adverse

family history may account for low educational attainment (see paragraph 3.2.2.). It is also possible that single status, homelessness, unemployment, educational problems and low socioeconomic standing are the consequence of habitual substance use, violence or severe psychotic symptomatology (see paragraphs 3.2.3. and 3.2.5.). Males tend to report more substance use than females, potentially mediating the relationship between gender and violence (Erkiran et al., 2006). Symptom severity could explain past hospitalization. On the other hand, past hospitalization may also be a sign of violent conduct, since this is often a reason or requisite for admission (Volavka & Citrome, 2008; Walsh, et al., 2002). Past conviction of violent crime may represent a patient's violent disposition (Modestin, 1998). At the same time, mentally ill offenders are disproportionately represented in the criminal justice system (Markowitz, 2011). Furthermore, familiarity with the authorities imaginably enhances the risk that someone will be convicted again or to longer prison terms.

3.2.2. Social factors

Psychotic patients who display violent behavior relatively often come from disadvantaged families with histories of criminality, substance use and (physical and sexual) maltreatment (Fazel, Grann et al., 2009; Mullen, 2006; Tiihonen et al., 1997; Witt et al., 2013). These circumstances may lead to adult violence or substance use through processes of social learning or genetic influence (Akers, 1998; Fazel, Grann et al., 2009). Violent patients are likely to reside in socially disorganized neighborhoods, characterized by high rates of low-income residents, ethnic diversity, norms approving of violence, little social cohesion and a lack of both informal and formal social control (Hiday, 1997; Markowitz, 2011; Mullen, 2006). This type of environment increases the likelihood of criminal victimization and other negative life events, such as unemployment and divorce (Hiday, 1997). In addition, the patient's immediate social

environment is often unsupportive (Haddock & Shaw, 2008). These stressful living conditions may increase the risk of violence directly or indirectly, through substance use or exacerbated psychopathology (Gregg, Barrowclough & Haddock, 2007; Hiday, 1997; Markowitz, 2011; Volavka & Citrome, 2011). Hypothetically, they could also be the result of the patient's violent conduct or severe psychotic symptomatology.

3.2.3. Persecutory delusions and command hallucinations

To reliably infer a causal relationship, it is crucial not only to establish the mere presence of psychosis, but also the onset and oscillation of symptoms in relation to violent behavior across a patient's life. After all, even if established before the occurrence of violence, a diagnosis of psychosis may have little predictive value when both events are temporally remote (Douglas et al., 2009). Moreover, it tells us nothing about the relative importance of specific symptoms. Unfortunately, this information is seldom recorded in studies (Douglas et al., 2009). For that reason, theories implicating psychotic symptoms as causes of violence should be treated with caution.

In terms of psychotic symptoms, persecutory delusions and command hallucinations have usually shown the strongest correlation with violent behavior (Angermeyer, 2000; Bjørkly, 1997; Bo et al., 2011; Fresan et al., 2005; Fresan, Apiquian & Nicolini, 2011; Hodgins et al., 2003; Joyal et al., 2007; Markowitz, 2011; Taylor, 1998; Taylor, 2008; Volavka & Citrome, 2008). Mediation is likely, however, since both symptoms are common in all psychotic patients (Bjørkly, 2002a; Bjørkly, 2002b; Cheung, Schweitzer, Crowley & Tuckwell, 1997; Fresan et al., 2011; Taylor, 1998; Volavka, 2013; Walsh et al., 2002). There is an increasing body of evidence suggesting that delusional violence is often prompted by associated emotional responses, such as anxiety, fear and anger (Bjørkly, 2002a; Bo et al., 2011; Cheung et al., 1997; Coid et al.,

2013; Elbogen & Johnson, 2009; Fanning, Berman, Mohn & McCloskey, 2011; Fresan et al., 2011; Haddock & Shaw, 2008; Hodgins, 2008; Stompe, Ortwein-Swoboda & Schanda, 2004). However, it is important to note that these emotions could also be a sign of deficient illness insight (Bjørkly, 2006). Possible mediating features of command hallucinations include the perceived consequences of disobedience, the significance attributed to the command and the patient's attitude toward the voice's identity (Barrowcliff & Haddock, 2006; Taylor, 2008). It is also possible that stress, as a consequence of violent behavior, elicits or exacerbates psychotic symptoms (Bjørkly, 2006; Douglas et al., 2009).

3.2.4. Comorbid antisocial personality pathology

Comorbid antisocial personality pathology has consistently been found to increase the risk of violence in psychosis. This applies particularly to diagnoses of conduct disorder[2] (CD), antisocial personality disorder (APD) and psychopathy (Belli & Ural, 2012; Bo et al., 2011; Douglas et al., 2009; Goethals, Vorstenbosch & van Marle 2008; Haddock & Shaw, 2008; Hodgins, Cree, Alderton & Mak, 2008; Hodgins, Tiihonen & Ross, 2005; McGregor, Castle & Dolan, 2012; Moran et al., 2003; Moran & Hodgins, 2004; Rogers & Fahy, 2008; Swanson et al., 2006; Taylor, 2008; Tengström, Grann, Långström & Kullgren, 2000; Tengström et al., 2004; Volavka, 2013; Volavka & Citrome, 2008 ; Volavka & Citrome, 2011; Witt et al., 2013). In broad terms, antisocial personality pathology is characterized by a disregard for social norms, deceitfulness, impulsivity, remorselessness and lack of empathy[3] (APA, 2013; Bo et al., 2011;

[2] While strictly not a personality disorder according to the DSM-5 classification, the criteria for CD correspond greatly with those for APD. This is reflected by the fact that diagnosed CD is a criterion for APD.

[3] The DSM-5 also includes aggressive behavior as criterion for CD and ADP. This feature is omitted here, because it is not part of psychopathy definitions and renders the relationship with violence tautological (Bo et al., 2011).

Volavka & Citrome, 2008). These personality characteristics may lead to violence in several ways. Firstly, they lower the patient's threshold to behave violently. They also make patients prone to substance use and treatment non-adherence (Goethals et al., 2008; Moran & Hodgins, 2004; Volavka & Citrome, 2011). Lastly, antisocial conduct may negatively affect the patient's social functioning (Bo et al., 2011).

Comorbid antisocial personality pathology and symptoms of delusions and hallucinations have been found to predict violence independently, implying the existence of two distinct etiologies of violence in psychosis (Hodgins, 1995; Hodgins et al., 2005; McGregor et al., 2011; Moran et al., 2003; Moran & Hodgins, 2004; Swanson et al., 2008; Tengström et al., 2004; Volavka, 2013; Volavka & Citrome, 2008). Patients with comorbid antisocial personality pathology usually display a lifelong pattern of persistent and versatile criminal conduct that commenced before the onset of illness. Violent behavior by these patients is thought to be predominantly associated with neurobiological abnormalities (see paragraph 3.2.8.), substance use and histories of parental criminality and childhood maltreatment. In contrast, violence in patients without comorbid antisocial personality pathology is hypothesized to be primarily motivated by paranoid delusions and command hallucinations. These patients should, as a consequence, typically act violently during periods of florid psychosis (Goethals et al., 2008; Hodgins et al., 2003; Hodgins et al., 2005; Moran & Hodgins, 2004).

3.2.5. Substance use

Substance use is widely regarded as a major predictor for violence in psychosis (Angermeyer, 2000; Bo et al., 2011; Cheung & Schweitzer, 1998; Dumais et al., 2011; Elbogen & Johnson, 2009; Erkiran et al., 2006; Goethals et al., 2008; Modestin, 1998; Soyka, 2000; Walsh et al., 2002; Witt et al., 2013). This seemingly applies to any type of substance (Witt et al., 2013).

There may be a number of ways in which substance use increases the risk of violent behavior. Through their neurobiological effects, substances reduce the patient's inhibitions (Hodgins, 2008; Volavka & Citrome, 2011). Substance use may also have a detrimental impact on the patient's social support system (Gregg et al., 2007). Furthermore, the buying and selling of illegal drugs commonly takes place in criminogenic environments (Hodgins, 2008). Certain drugs also aggravate psychotic symptoms. This is especially true for cannabis (Gregg et al., 2007). Paradoxically, the use of substances may simultaneously be a patient's attempt to alleviate psychotic symptoms or feelings of depression and anxiety (Gregg et al., 2007).

3.2.6. Inadequate insight

Insight in mental disorder is defined as the patient's recognition of illness, its symptoms and consequences, and the need for treatment (Bjørkly, 2006). Inadequate insight has frequently been suggested as a risk factor for violent behavior in psychotic patients (Alia-Klein, O'Rourke, Goldstein & Malaspina, 2007; Buckley et al., 2004; Calatayud et al., 2012; Mullen 2006; Nederlof et al., 2013; Witt et al., 2013). However, studies on this subject are scarce and their results inconclusive (Bjørkly, 2006; Lincoln & Hodgins, 2008). Perhaps a strong belief that delusions or hallucinations are real increases the probability that the patient acts on them (Bjørkly, 2006). Denial of illness or the need for psychiatric care may also bring about violent behavior through non-adherence to treatment (Bjørkly, 2006; Lincoln & Hodgins, 2008; Volavka & Citrome, 2011).

3.2.7. Treatment non-adherence

Non-adherence to therapy and medication is associated with an elevated risk of violence in psychotic individuals (Alia-Klein et al., 2007; Bo et al., 2011; Belli & Ural, 2012; Volavka, 2013; Witt et al., 2013). There are several explanations for this finding. By refusing antipsychotic medication, psychotic symptoms do not diminish or even worsen (Volavka & Citrome, 2011). Patients with persecutory delusions may be reluctant to comply with treatment, due to fear and suspicion of mental health professionals (Freeman & Garety, 2006). Lastly, treatment non-adherence appears to be associated with substance use (Hodgins, 2008; Swartz et al., 1998; Volavka & Citrome, 2011). This association may be reciprocal, with non-adherence inducing self-medication and substance use interfering with treatment (Swartz et al., 1998).

3.2.8. Physiological factors

While still a relatively new area of research, there is some evidence to suggest that physiological factors are integral to the etiology of violent behavior in psychosis, particularly schizophrenia. The most consistent findings point to a low-activity polymorphism of the gene encoding catechol-O-methyltransferase (COMT), an enzyme involved in dopamine metabolism, serotonin hypofunction and frontal and temporal lobe abnormalities (Cheung & Schweitzer, 1998; Hoptman & Antonius, 2011; Naudts & Hodgins, 2006; Soyka, 2011; Volavka, 2013; Volavka & Citrome, 2011). A positive association has also been observed between violence and medication side effects, most notably akathisia and neuroleptic-induced deficit syndrome (Cheung & Schweitzer, 1998; Mullen, 2006). These conditions are hypothesized to make the patient prone to violence by hampering the experience and recognition of emotions, lowering stress reactivity, increasing impulsivity and creating cognitive biases that favor aggressive responses to stressful

or provocative situations (Naudts & Hodgins, 2006; Seo & Patrick, 2008; Weiss, 2012). Impairment of cognitive functions may also explain the patient's educational problems and susceptibility to substance use (Seo & Patrick, 2008; Weiss, 2012). Overactive mesolimbic dopaminergic projections have been suggested to be responsible for the increased severity of delusions and hallucinations found in aggressive patients (Soyka, 2011). Finally, unpleasant side effects of medication may bring the patient to discontinue intake (Swartz et al., 1998).

3.2.9. Summary

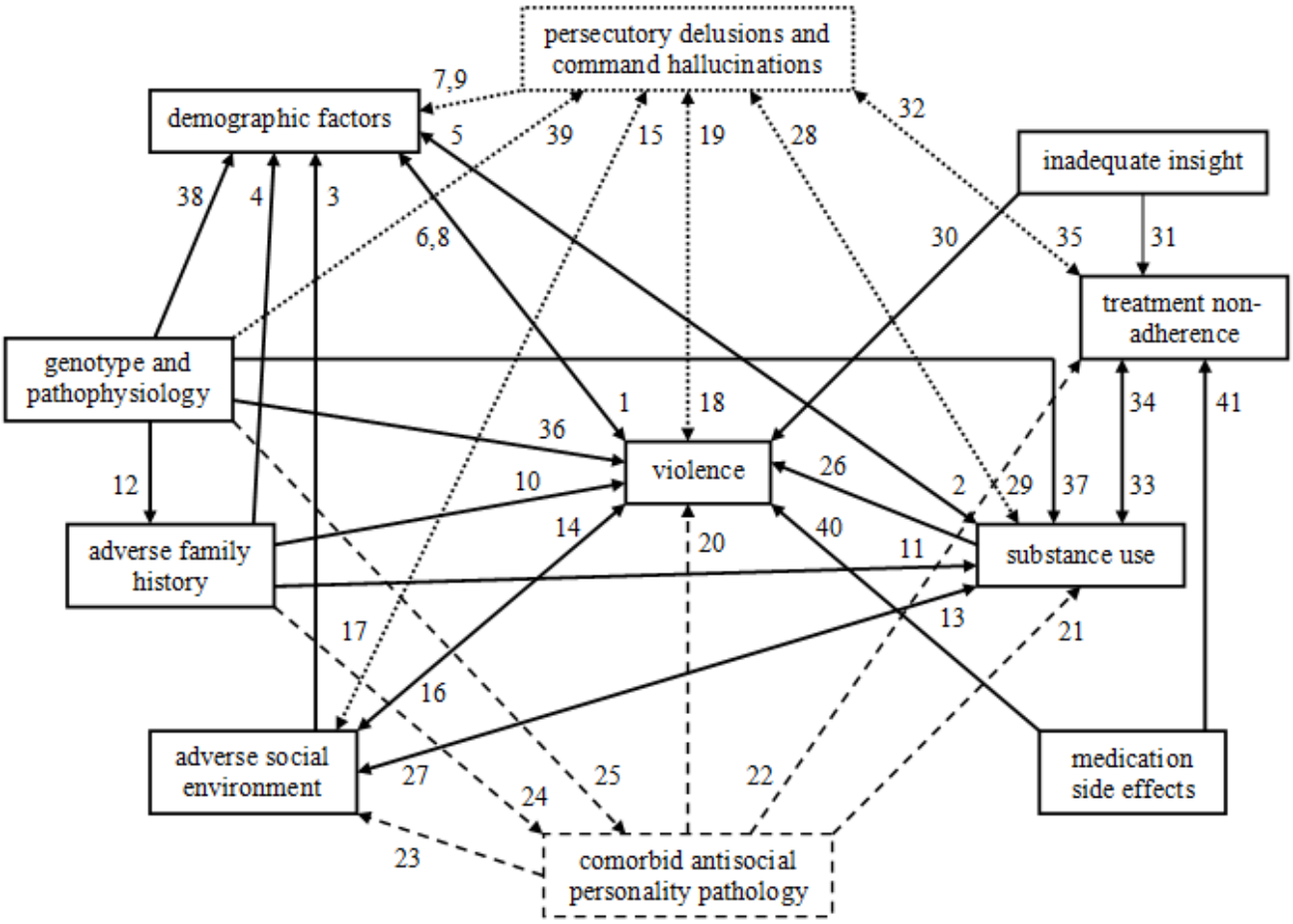
Violent behavior in psychosis is etiologically complex. It may be caused by numerous interacting risk factors. Possible causal pathways between these risk factors and violence, as described in the preceding sections, are summarized below and schematically depicted in figure 1. The numbers assigned to each line correspond to those of each hypothesis. The arrows indicate direction. Causal pathways associated with comorbid antisocial personality pathology are represented by dashed lines. Dotted lines signify causal pathways associated with persecutory delusions and command hallucinations.

Certain demographic descriptors may be directly or indirectly related to violence in psychotic patients. Low self-control associated with being male or young of age predisposes the patient toward violent behavior (1). Males also tend to use substances more frequently than females (2). Low socioeconomic status and unemployment may reflect a high degree of social disorganization in the patient's area of residence (3), while an adverse family history potentially accounts for low educational attainment (4). Habitual substance use possibly explains the patient's single status, homelessness, unemployment, educational adversities and low economic standing (5). Single status, homelessness, unemployment, educational problems, low socioeconomic standing and past hospitalization may be caused by the patient's recurrent

violent behavior (6) or severe psychotic symptoms (7). Besides being an indicator of violent conduct (8), one or more previous convictions of violent offenses may reflect the patient's vulnerability for processing through the criminal justice system (9).

Crime and maltreatment by family members could lead to later violence by way of social learning (10). Familial transmission of substance use is similarly conceivable (11). An adverse family history may also point to the influence of genetic factors (12).

Figure 1. Possible causal pathways between risk factors and violence in psychosis



An adverse social environment, defined as living in a socially disorganized neighborhood and a lack of social support, may promote substance use (13), give rise to violence (14) and exacerbate psychotic symptoms (15). Alternatively, these circumstances may be a consequence of the patient's violent conduct (16) or severe psychotic symptomatology (17).

A patient's violent behavior may be propelled by certain features of persecutory delusions and command hallucinations (18). It is also possible that psychotic symptoms are aggravated or elicited by stress that accompanies acts of violence (19).

Comorbid antisocial personality pathology underlies an inclination toward violence (20), substance use (21) and treatment non-adherence (22). Persistent antisocial conduct could also explain a negative social environment (23). Antisocial personality pathology often emanates from an adverse family history (24) and neurobiological factors that are believed to be conducive to violence (25).

Substance use may cause violence directly through diminished behavioral control (26) or indirectly, either by placing the patient in a criminogenic and unsupportive social environment (27) or by aggravating psychotic symptoms (28). The patient may also use substances in an attempt to relieve psychotic symptoms (29).

Inadequate insight potentially leads to violence when the patient believes delusions or hallucinations are real (30) or to treatment non-adherence when the patient denies being ill or in need of psychiatric care (31).

Treatment non-adherence may be related to violent behavior in several ways. Psychotic symptoms continue or worsen without antipsychotic medication (32). In the absence of proper treatment, the patient may use substances as a means of self-medication (33). At the same time, substance use impedes successful treatment (34). Finally, persecutory delusions can cause patients to be fearful and suspicious of mental health professionals and, as a consequence, oppose treatment (35).

Increased dopaminergic neurotransmission related to a low-activity polymorphism of the COMT gene and other forms of pathophysiology, such as serotonin hypofunction and abnormalities in the frontotemporal circuitry, predispose the patient toward violent behavior (36) and substance use (37) by impairing emotional and cognitive functions. Cognitive deficits may also explain the patient's low educational attainment (38). A hyperactive mesolimbic dopamine system could underlie the presence of severe symptoms of delusions and hallucinations (39). Medication side effects may make the patient susceptible to violence (40) or cause intake discontinuation (41).

4. Discussion

While proven statistically robust, the association between psychosis and violence still cannot be causally explained. This is partially due to methodological aspects of research, which include study design, sampling, operationalization of violence and psychosis and confounding factors. Above all, the complex etiology of violent behavior in psychosis renders it difficult to establish a causal relationship between the two. Its manifestation may indeed be caused by numerous risk factors, several of which are mutually related: demographics, social factors, persecutory delusions, command hallucinations, comorbid antisocial personality pathology, substance use, lack of insight, treatment non-adherence and physiological factors. This study has attempted to conceptualize the causal relationship between violence and psychosis by proposing 41 potential causal pathways between these risk factors and violent behavior. To the authors' knowledge, this constitutes the most comprehensive overview of hypotheses regarding violence in psychosis to date.

Some limitations of the present study should be noted. Firstly, though extensive, the selection of literature used for this review is not exhaustive. Secondly, the methodological quality of the

included studies was not systematically weighted for analysis. We have aimed to counterbalance these limitations by emphasizing the findings of previous reviews. However, the primary aim of this review is to conceptualize the associations between risk factors and violence in psychosis, not to quantify them or to evaluate the empirical evidence.

In conclusion, the current review holds several implications for research and practice. It has the potential to stimulate research on violence in psychosis by providing future studies with a comprehensive hypothetical and interpretative framework. The review also identifies a number of urgent avenues of investigation. In particular, the role of persecutory delusions and command hallucinations as potential causes of violence requires further investigation. This is only possible by evaluating the fluctuation of these symptoms in relation to violent behavior over time. Furthermore, studies should consider violence associated with florid psychotic symptoms as etiologically different from that associated with comorbid antisocial personality pathology. More research is also needed on the genetic, neurological and biochemical underpinnings of violence in psychosis. In addition to investigating the role of specific risk factors, researchers are encouraged to include measures for as many risk factors as possible to minimize the number of confounding factors and maximize the comparability of study results. Methodological implications arise from our review as well. More cohort studies should be conducted to determine whether the associations between risk factors and violence are causal rather than correlational. Community and institutional samples should be combined to optimize the external validity of studies. Appropriate external control subjects, such as siblings, may serve to enhance the findings' internal validity. For reliable and valid measurement, psychosis should be evaluated at symptom-level using structured interviews, whereas collection of data on violent behavior should combine criminal records, case notes, collateral information and self-report measures. A universal definition of violence should be agreed upon to facilitate comparison of results across studies. Finally, additional meta-analyses are needed to estimate the extent of publication bias in the field. By clarifying the current understanding of violent behavior in

psychosis, this review contributes to the improvement of its prevention and treatment, dispelling the stigma associated with psychosis and the strengthening of the patient's legal position.

Funding acknowledgements

This research was carried out without specific funding from any public, private or voluntary organization.

References

Akers, R. (1998). Social learning and social structure. A general theory of crime and deviance. Boston: Northeastern University Press.

Alia-Klein, N., O'Rourke, T. M., Goldstein, R. Z., & Malaspina, D. (2007). Insight into illness and adherence to psychotropic medications are separately associated with violence severity in a forensic sample. Aggressive Behavior, 33(1), 86-96.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.

Angermeyer, M. C. (2000). Schizophrenia and violence. Acta Psychiatrica Scandinavica, 102(407), 63-67.

Arseneault, L., Cannon, M., Murray, R., Poulton, R., Caspi, A., & Moffitt, T. E. (2003). Childhood origins of violent behaviour in adults with schizophreniform disorder. The British Journal of Psychiatry, 183(6), 520-525.

Barrowcliff, A. L., & Haddock, G. (2006). The relationship between command hallucinations and factors of compliance. A critical review of the literature. The Journal of Forensic Psychiatry & Psychology, 17(2), 266-298.

Belli, H., & Ural, C. (2012). The association between schizophrenia and violent or homicidal behaviour. The prevention and treatment of violent behaviour in these patients. West Indian Medical Journal, 61(5), 538-543.

Bjørkly, S. (1997). Clinical assessment of dangerousness in psychotic patients. Some risk indicators and pitfalls. Aggression and Violent Behavior, (2)2, 167-178.

Bjørkly, S. (2002). Psychotic symptoms and violence toward others – a literature review of some preliminary findings. Part 1. Delusions. Aggression and Violent Behavior, 7(6), 617-631.

Bjørkly, S. (2002). Psychotic symptoms and violence toward others – a literature review of some preliminary findings. Part 2. Hallucinations. Aggression and Violent Behavior, 7(6), 605-615.

Bjørkly, S. (2006). Empirical evidence of a relationship between insight and risk of violence in the mentally ill – a review of the literature. Aggression and Violent Behavior, 11(4), 414-423.

Bo, S., Abu-Akel, A., Kongerslev, M., Haahr, U. H., & Simonsen, E. (2011). Risk factors for violence among patients with schizophrenia. Clinical Psychology Review, 31(5), 711-726.

Buckley, P. F., Hrouda, D. R., Friedman, L., Noffsinger, S. G., Resnick, P. J., & Camlin-Shingler, K. (2004). Insight and its relationship to violent behavior in patients with schizophrenia. The American Journal of Psychiatry, 161(9), 1712-1714.

Calatayud, G. L., Sebastián, N. H., García- Iturrospec, E. A., Piqueras, J. C. G., Arias, J. S., & Cercós, C. L. (2012). Relationship between insight, violence and diagnoses in psychotic patients. Revista de Psiquiatría y Salud Mental, 5(1), 43-47.

Cheung, P., Schweitzer, I., Crowley, K., & Tuckwell, V. (1997). Violence in schizophrenia. Role of hallucinations and delusions. Schizophrenia Research, 26(2), 181-190.

Cheung, P., & Schweitzer, I. (1998). Correlates of aggressive behaviour in schizophrenia. An overview. Australian and New Zealand Journal of Psychiatry, 32(3), 400-409.

Coid, J. W., Ullrich, S., Kallis, C., Keers, R., Barker, D., Cowden, F., & Stamps, R. (2013). The relationship between delusions and violence. Findings from the East London first episode psychosis study. JAMA Psychiatry, 70(5), 465-471.

Cronin, P., Ryan, F., & Coughlan, M. (2008). Undertaking a literature review. A step-by-step approach. British Journal of Nursing, 17(1), 38-43.

Douglas, K. S., Guy, L. S., & Hart, S. D. (2009). Psychosis as a risk factor for violence to others. A meta-analysis. Psychological Bulletin, 135(6), 679-706.

Dumais, A., Potvin, S., Joyal, C. C., Allaire, J.- F., Stip, E., Lesage, A., . . . Côté, G. (2011). Schizophrenia and serious violence. A clinical-profile analysis incorporating impulsivity and substance-use disorders. Schizophrenia Research, 130(1), 234-237.

Elbogen, E. B., & Johnson, S. C. (2009). The intricate link between violence and mental disorder. Results from the National Epidemiologic Survey on Alcohol and Related Conditions. Archives of General Psychiatry, 66(2), 152-161.

Erkiran, M., Özüalan, H., Evren, C., Aytaçlar, S., Kirisci, L., & Tarter, R. (2006). Substance abuse amplifies the risk for violence in schizophrenia spectrum disorder. Addictive Behaviors, 31(10), 1797-1805.

Fanning, J. R., Berman, M. E., Mohn, R. S., & McCloskey, M. S. (2011). Perceived threat mediates the relationship between psychosis proneness and aggressive behavior. Psychiatry Research, 186(2), 210-218.

Fazel, S., Grann, M., Carlström, E., Lichtenstein, P., & Långström, N. (2009). Risk factors for violent crime in schizophrenia. A national cohort study of 13,806 patients. Journal of Clinical Psychiatry, 70(3), 362-369.

Fazel, S., Gulati, G., Linsell, L., Geddes, J. R., & Grann, M. (2009). Schizophrenia and violence. Systematic review and meta- analysis. PLoS Medicine, 6(8), 1-14.

Fazel, S., Långström, N., Hjern, A., Grann, M., & Lichtenstein, P. (2009). Schizophrenia, substance abuse, and violent crime. JAMA Psychiatry, 301(19), 2016-2023.

Freeman, D., & Garety, P. (2006). Helping patients with paranoid and suspicious thoughts. A cognitive–behavioural approach. Advances in Psychiatric Treatment 12(6), 404-441.

Fresan, A., Apiquian, R., Fuente-Sandoval, C. de la, Loyzaga, M., García-Anaya, C., Meyenberg, N., & Nicolini, H. (2005). Violent Behavior in schizophrenic patients. Relationship with clinical symptoms. Aggressive Behavior, 31(6), 511-520.

Fresan, A., Apiquian, R., & Nicolini, H. (2011). Psychotic symptoms and the prediction of violence in schizophrenic patients. In D. P. French (Ed.), Schizophrenic psychology. New research (pp. 239-254). New York, NY: Nova Science Publishers.

Goethals, K. R., Vorstenbosch, E. C. W., & Marle, H. J. C. van (2008). Diagnostic comorbidity in psychotic offenders and their criminal history. A review of the literature. International Journal of Forensic Mental Health, 7(2), 147-156.

Gottfredson, M. R., & Hirschi, T. (1990). A general theory of crime. Stanford, CA: Stanford University Press.

Gregg, L., Barrowclough, C., & Haddock, G. (2007). Reasons for increased substance use in psychosis. Clinical Psychology Review, 27(4), 494–510.

Haddock, G., & Shaw, J. J. (2008). Understanding and working with aggression, violence, and psychosis. In K. T. Mueser & D. V. Jeste (Eds.), Clinical handbook of schizophrenia (pp. 398-410). New York, NY: The Guilford Press.

Hiday, V. A. (1997). Understanding the connection between mental illness and violence. International Journal of Law and Psychiatry, 20(4), 399-417.

Hodgins, S. (1995). Major mental disorder and crime. An overview. Psychology, Crime and Law, 2(1), 5-17.

Hodgins, S. (2008). Violent behaviour among people with schizophrenia. A framework for investigations of causes, and effective treatment, and prevention. Philosophical Transactions of the Royal Society of London. Series B, 363(1503), 2505-2518.

Hodgins, S., Cree, A., Alderton, J., & Mak, T. (2008). From conduct disorder to severe mental illness. Associations with aggressive behaviour, crime and victimization. Psychological Medicine, 38(7), 975-987.

Hodgins, S., Hiscoke, U. L., & Freese, R. (2003). The antecedents of aggressive behavior among men with schizophrenia. A prospective investigation of patients in community treatment. Behavioral Sciences and the Law, 21(4), 523-546.

Hodgins, S., Tiihonen, J., & Ross, D. (2005). The consequences of conduct disorder for males who develop schizophrenia. Associations with criminality, aggressive behavior, substance use, and psychiatric services. Schizophrenia Research, 78(2), 323-335.

Hoptman, M. J., & Antonius, D. (2011). Neuroimaging correlates of aggression in schizophrenia. An update. Current Opinion in Psychiatry, 24(2), 100-106.

Joyal, C. C., Dubreucq, J.-L., Gendron, C., & Millaud, F. (2007). Major mental disorders and violence. A critical update. Current Psychiatry Reviews, 3(1), 33-50.

Lincoln, T. M., & Hodgins, S. (2008). Is lack of insight associated with physically aggressive behavior among people with schizophrenia living in the community? The Journal of Nervous and Mental Disease, 196(1), 62-66.

Mann, C. J. (2003). Observational research methods. Research design II. Cohort, cross sectional, and case-control studies. Emergency Medicine Journal, 20(1), 54-60.

Marriot, C., Hamilton-Giachritsis, C., & Harrop, C. (2013). Factors promoting resilience following childhood sexual abuse. A structured, narrative review of the literature. Child Abuse Review, (23)1, 17-34.

Markowitz, F. E. (2011). Mental illness, crime, and violence. Risk, context, and social control. Aggression and Violent Behavior, 16(1), 36-44.

McGregor, K., Castle, D., & Dolan, M. (2012). Schizophrenia spectrum disorders, substance misuse, and the four-facet model of psychopathy. The relationship to violence. Schizophrenia Research, 136(1), 116-121.

Modestin, J. (1998). Criminal and violent behavior in schizophrenic patients. An overview. Psychiatry and Clinical Neurosciences, 52(6), 547-554.

Modestin, J., & Wuermle, O. (2005). Criminality in men with major mental disorder with and without comorbid substance use. Psychiatry and Clinical Neurosciences 59(2), 5-29.

Moran, P., & Hodgins, S. (2004). The correlates of comorbid antisocial personality disorder in schizophrenia. Schizophrenia Bulletin, 30(4), 791-802.

Moran, P., Walsh, E., Tyrer, P., Burns, T., Creed, F., & Fahy, T. (2003). Impact of comorbid personality disorder on violence in psychosis. Report from the UK700 trial. The British Journal of Psychiatry, 181(2), 129-134.

Mullen, P. E. (2006). Schizophrenia and violence. From correlations to preventive strategies. Advances in Psychiatric Treatment, 12(3), 239-248.

Naudts, K., & Hodgins, S. (2006). Neurobiological correlates of violent behavior among persons with schizophrenia. Schizophrenia Bulletin, 32(3), 562-572.

Nederlof, A. F., Muris, P., & Hovens, J. E. (2013). The epidemiology of violent behavior in patients with a psychotic disorder. A systematic review of studies since 1980. Aggression and Violent Behavior, 18(1), 83-189.

Rogers, T., & Fahy, T. (2008). Suicide, violence, and schizophrenia. Psychiatry, 7(11), 482-486.

Seo, D., & Patrick, C. J. (2008). Role of serotonin and dopamine system interactions in the neurobiology of impulsive aggression and its comorbidity with other clinical disorders. Aggression and violent behavior, 13(5), 383-395.

Soyka, M. (2000). Substance misuse, psychiatric disorder and violent and disturbed behaviour. The British Journal of Psychiatry, 176(4), 345-350.

Soyka, M. (2011). Neurobiology of aggression and violence in schizophrenia. Schizophrenia Bulletin 37(5), 913-920.

Sternberg, R. J., Roediger, H. L., & Halpern, D. F. (2007). Critical thinking in psychology. New York, NY: Cambridge University Press.

Stompe, T., Ortwein-Swoboda, G., & Schanda, H. (2004). Schizophrenia, delusional symptoms, and violence. The threat/control- override concept reexamined. Schizophrenia Bulletin, 30(1), 31-44.

Swanson, J. W., Dorn, R. A. van, Swartz, M. S., Smith, A., Elbogen, E. B., & Monahan, J. (2008). Alternative pathways to violence in persons with schizophrenia. The role of childhood antisocial behavior problems. Law and Human Behavior, 32 (3), 228-240.

Swanson, J. W., Swartz, M. S., Dorn, R. A. van, Elbogen, E. B., Wagner, H. R., Rosenheck, R. A., . . . Lieberman, J. A. (2006). A national study of violent behavior in persons with schizophrenia. Archives of General Psychiatry, 63(5), 490-499.

Swartz, M. S., Swanson, J. E., Hiday, V. A., Borum, R., Wagner, H. R., & Burns, B. J. (1998). Violence and severe mental illness. The effects of substance abuse and nonadherence to medication. The American Journal of Psychiatry, 155(2), 226-231.

Taylor, P. J. (1998). When symptoms of psychosis drive serious violence. Social Psychiatry and Psychiatric Epidemiology, 33(1), 47-54.

Taylor, P. J. (2008). Psychosis and violence. Stories, fears, and reality. Canadian Journal of Psychiatry, 53(10), 647-659.

Tengström, A., Grann, M., Långström, N., & Kullgren, G. (2000). Psychopathy (PCL-R) as a predictor of violent recidivism among criminal offenders with schizophrenia. Law and Human Behavior, 24(1), 45-58.

Tengström, A., Hodgins, S., Grann, M., Långström, N., & Kullgren, G. (2004). Schizophrenia and criminal offending. The role of psychopathy and substance use disorders. Criminal Justice and Behavior, 31(4), 367-391.

Tiihonen, J., Isohanni, M., Räsänen, P., Koiranen, M., & Moring, J. (1997). Specific major mental disorders and criminality. A 26-year prospective study of the 1966 Northern Finland birth cohort. The American Journal of Psychiatry, 154(6), 840-845.

Volavka, J. (2013). Violence in schizophrenia and bipolar disorder. Psychiatria Danubina, 25(1), 24-33.

Volavka, J., & Citrome, L. (2008). Heterogeneity of violence in schizophrenia and implications for long-term treatment . International Journal of Clinical Practice, 62(8), 1237-1245.

Volavka, J. & Citrome, L. (2011). Pathways to aggression in schizophrenia affect results of treatment. Schizophrenia Bulletin, 37(5), 921-929.

Wallace, C., Mullen, P. E., & Burgess, P. (2004). Criminal offending in schizophrenia over a 25-year period marked by deinstitutionalization and increasing prevalence of comorbid substance use disorders. The American Journal of Psychiatry, 161(4), 716–727.

Walsh, E., Buchanan, A., & Fahy, T. (2002). Violence and schizophrenia. Examining the evidence. The British Journal of Psychiatry, 180(6), 490-495.

Weiss, E. M. (2012). Neuroimaging and neurocognitive correlates of aggression and violence in schizophrenia. Scientifica, *2012. doi: 10.6064/2012/158646*

Witt, K., Dorn, R. A. van, & Fazel, S. (2013). Risk factors for violence in psychosis. Systematic review and meta-regression analysis of 110 studies. PLoS ONE, 8(2), 1-15.